

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460



OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

February 02, 2022

Memorandum:

Subject: Acute Toxicity Review for EPA File Symbol: 33427-RT

Applicant: Aceto US, L.L.C.
Product Name: Aceto Acetamiprid Technical
DP Barcode: D461820
Decision No.: 570713
Action Code: R334
PC Code(s): 099050 (Acetamiprid)

From: Odbert Triplett, Biologist
Chemistry, Inerts and Toxicology Assessment Branch (CITAB)
Registration Division (7505P)

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Formulation from label:

<u>Active Ingredient(s):</u>	<u>% by wt.</u>
Acetamiprid, (E)-N1-[(6-chloro-3-pyridyl)methyl]- N2-cyano-N1-methylacetamidine.....	99.5%
<u>Other Ingredients:</u>	0.5%
Total:	100.00%

ACTION REQUESTED: The Risk Manager requests a review of acute toxicity studies submitted to support registration of Aceto Acetamiprid Technical, EPA File Symbol: 33427-RT.

BACKGROUND: The registrant, Aceto US, L.L.C., has applied to register Aceto Acetamiprid Technical, EPA File Symbol: 33427-RT. The form 8570-1 (OMB 2070-0060, dated January 27, 2021) cites 8033-20 as similar or identical. The proposed product contains the active ingredients Acetamiprid (99.5%). The following MRIDs have been submitted for review: 51437712 (870.1100), 51437713 (870.1200), 51437714 (870.1300), 51437715 (870.2400), 51437716 (870.2500) and 51437717 (870.2600).

The Agency reviewed the data to assess the acute toxicity, irritation, and dermal sensitization potential of the proposed product (see Toxicity Profile under "Comments and Recommendations"). Aceto Acetamiprid Technical, EPA File Symbol: 33427-RT, is a new MUP product with unregistered source(s) of active ingredient(s); The label of Aceto Acetamiprid Technical, EPA File Symbol: 33427-RT, indicates that it is "For Manufacturing or Formulating Use Only."

The application package includes a copy of the proposed Basic CSF dated January 21, 2021 with the Agency notation "Technical & water only, no inerts to review."

RECOMMENDATIONS:

1. The registrant has used the phrase " May be fatal if swallowed, absorbed through the skin, or inhaled" which needs to be corrected to avoid confusion to "May be fatal if swallowed. Harmful if absorbed through skin" the correct eye irritation (Cat. IV) precautionary text would be "Causes moderate eye irritation". See page Three.
2. All acute toxicity data requirements for the registration of Aceto Acetamiprid Technical, EPA File Symbol: 33427-RT have been satisfied by the submitted studies (MRIDs 51437712-17).
3. The proposed Basic CSF submitted for Aceto Acetamiprid Technical, EPA File Symbol: 33427-RT (01/25/2021) must be reviewed and accepted by the product chemists in the Chemistry, Inerts and Toxicology Assessment Branch.
4. The registrant has added optional first aid statements for "if inhaled" and "if in eyes." These are acceptable.
5. The proposed precautionary and first aid labeling statements are consistent with those of the last (Feb. 6, 2020) accepted label for 8033-20. However, the phrase " May be fatal if swallowed, absorbed through the skin, or inhaled" needs to be corrected to "May be fatal if swallowed. Harmful if absorbed through skin." If the registrant wishes to address inhalation and eye exposure in the precautionary statements the inhalation statement would be "Harmful if inhaled" and the eye statement would be "Causes moderate eye irritation". See page Three.

6. The registrant has proposed the statement “Wear protective clothing and rubber gloves” consistent with the last accepted (February 6, 2020) label for 8033-20. The Agency preference for the glove specification would be for “waterproof” rather than “rubber.”
7. The registrant suggests that a respirator be worn. This is acceptable, although the Agency preference would be for a “dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C)” (40 CFR 156.212(g)). The registrant has added the precautionary text “Do not breathe dust” which is acceptable.
8. The registrant has added a “symptoms of poisoning” section and this is acceptable.
9. The following constitutes the toxicology profile assigned to Aceto Acetamiprid Technical, EPA File Symbol: 33427-RT:

Acute oral toxicity	acceptable	II	MRID	51437712
Acute dermal toxicity	acceptable	III	MRID	51437713
Acute inhalation toxicity	acceptable	IV	MRID	51437714
Primary eye irritation	acceptable	IV	MRID	51437715
Primary dermal	acceptable	IV	MRID	51437716
Dermal sensitization	acceptable	negative	MRID	51437717

Based on the acute toxicity profile given above, the following are the precautionary and first aid labeling statements for Aceto Acetamiprid Technical, EPA File Symbol: 33427-RT, as obtained from the Label Review System:

Product ID: 33427-RT

Product Name: Aceto Acetamiprid Technical

Precautionary Statements:

Keep out of Reach of Children.

Signal Word: **WARNING**

Poison Label: **None**

The phrase “Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)” is acceptable

Hazards to Humans and Domestic Animals:

May be fatal if swallowed. Harmful if absorbed through skin.

Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Avoid contact with skin, eyes or clothing. Remove and wash contaminated clothing before reuse.

First Aid:

If swallowed:

- Call a poison control center or doctor immediately for treatment advice.
- Have person sip a glass of water if able to swallow.
- Do not induce vomiting unless told to do so by a poison control center or doctor.
- Do not give anything by mouth to an unconscious person.

If on skin or clothing:

- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor for treatment advice.

The Note to Physician suggested by the registrant is acceptable.

EPA encourages but does not require (see PR Notice 2001-1) registrants to include a company telephone number or toll-free hotline for emergency information in the first aid section. The following are examples of appropriate statements that may be included on the label:

Have the product container or label with you when calling a poison control center or doctor or going for treatment. For medical emergencies, call the poison control center at 1-800-222-1222. For general information about this product, call 1-XXX-XXX-XXXX [may include hours of service], or contact the National Pesticides Information Center (NPIC) at 1-800-858-7378, Monday through Friday, 8 AM to 12 PM PST, or at <http://npic.orst.edu>.

The proposed label includes a telephone number and a statement to have the product container and label when calling to a poison control center or doctor, along with a contact phone number for emergency medical information. These statements are appropriate and acceptable.

DATA EVALUATION RECORD

ACETO ACETAMIPRID TECHNICAL [ACETAMIPRID TC]

**STUDY TYPES: ACUTE ORAL TOXICITY - RAT [OCSPP 870.1100; OECD 423]
ACUTE DERMAL TOXICITY - RAT [OCSPP 870.1200; OECD 402]
ACUTE INHALATION TOXICITY - RAT [OCSPP 870.1300; OECD 403]
ACUTE EYE IRRITATION - RABBIT [OCSPP 870.2400; OECD 405]
ACUTE DERMAL IRRITATION - RABBIT [OCSPP 870.2500; OECD 404]
ACUTE DERMAL SENSITIZATION - GUINEA PIG [OCSPP 870.2600; OECD 406]**

MRIDs 51437712, 51437713, 51437714, 51437715, 51437716, and 51437717

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Task Order No. AcuteTox-4-97

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Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Summittec Corp. for the U.S. Environmental Protection Agency under Contract No. EP-W-16-019

DATA EVALUATION RECORD

Reviewers: Odbert Triplett, Biologist, CITAB
Susan S. Little, Ph.D., DABT (Summitec Corp.)

Date: February 02, 2022

Product Reg. No./File Symbol: 33427-RT

1. DP BARCODE: 461820				
2. PC CODE(S): 099050				
3. CURRENT DATE: February 02, 2022				
4. TEST MATERIAL: Acetamiprid TC: 99.5% a.i.; CAS # 135410-20-7; Batch No. RT2018111817; white powder; pH 6.15; density (from p. 20 of MRID 51437715 the weight of 0.1 mL compacted material was 60 mg); expiration date: November 17, 2020; stored at room temperature.				
Study/Species/Lab Study #/Date	MRID	Results	Tox Cat	Core Grade *
Acute oral toxicity/ Wistar rat (Acute Toxic Class Method) INTOX PVT. LTD. (Maharashtra, India) Study No. 18489 September 4, 2019 OCSPP 870.1100; OECD 423	51437712	LD₅₀ > 50 mg/kg bw and < 300 mg/kg bw; LD₅₀ cutoff value = 300 mg/kg bw 9 fasted female rats (3/step) were administered 300 mg/kg bw or 50 mg/kg bw test substance as 30 mg/mL or 5 mg/mL, respectively, suspensions in analytical grade water containing 0.2% Tween 80. Two of three animals administered 300 mg/kg bw were found dead at 4 hours or 1-day post-dosing after exhibiting tremors and hypoactivity. The surviving animal also exhibited tremors and hypoactivity but recovered by Day 7, appeared normal for the remainder of the study, and gained body weight during both study weeks. All animals administered 50 mg/kg bw survived, gained body weight during both study weeks, and appeared normal for the duration of the study. No gross	II	A

		abnormalities were observed in any animal at necropsy.		
<p>Acute dermal toxicity/ Wistar rat</p> <p>INTOX PVT. LTD. (Maharashtra, India) Study No. 18490 September 4, 2019</p> <p>OCSPP 870.1200; OECD 402</p>	51437713	<p>LD₅₀ > 2000 mg/kg bw</p> <p>3 female rats were dermally exposed for 24 hours to 2000 mg/kg bw of the test substance moistened with analytical grade water.</p> <p>All animals survived, appeared normal for the duration of the study, and gained body weight during both study weeks. No gross abnormalities were found at necropsy.</p> <p><u>Study deficiencies:</u> The volume of water used to moisten the test substance was not provided.</p>	III	A
<p>Acute inhalation toxicity/Wistar rat (4-hour, Nose-only)</p> <p>INTOX PVT. LTD. (Maharashtra, India) Study No. 18491 September 4, 2019</p> <p>OCSPP 870.1300; OECD 403</p>	51437714	<p>LC₅₀ > 3.69 mg/L (both sexes)</p> <p>6 rats (3/sex) were exposed to the test substance as received aerosolized at 3.69 mg/L.</p> <p>Mean gravimetric chamber conc.: 3.69 mg/L; Average MMAD: 1.45 µm; Average GSD: 2.72; Nominal conc.: 4.66 mg/L.</p> <p>All animals survived and gained body weight during both study weeks. All animals exhibited nasal discharge, abdominal breathing, hypoactivity, and ruffled appearance from hour 4 of exposure with resolution by Day 2, then appeared normal for the remainder</p>	IV	A

		of the study. No gross abnormalities were observed at necropsy.		
<p>Primary eye irritation/ New Zealand White rabbit</p> <p>INTOX PVT. LTD. (Maharashtra, India) Study No. 18493 September 4, 2019</p> <p>OCSPP 870.2400; OECD 405</p>	51437715	<p>MMTS and the descriptive (Kay and Calandra) rating cannot be determined.</p> <p>The test substance (0.1 mL = 60 mg) as received was instilled into the left eye of three female young adult rabbits. Eyes were rinsed with analytical grade water 1 hour after instillation. Each eye was anesthetized with proparacaine HCl, and systemic analgesia was provided.</p> <p>No iritis, corneal opacity, or chemosis was observed in any eye during the study. Discharge was not scored or recorded. At 1 hour post dose, all treated eyes exhibited conjunctival redness (grade = 1) which resolved by 24 hours.</p> <p>All animals appeared otherwise normal for the duration of the study and gained body weight.</p>	IV	A
<p>Primary dermal irritation/New Zealand White rabbit</p> <p>INTOX PVT. LTD. (Maharashtra, India) Study No. 18492 September 4, 2019</p> <p>OCSPP 870.2500; OECD 404</p>	51437716	<p>Non-Irritating; Mean irritation at 72 hrs = 0.0 PDII = 0.0</p> <p>Three male rabbits were exposed for 4 hours to 0.5 g of the test substance moistened with analytical grade water.</p> <p>No erythema or edema was seen during the study. All animals appeared normal for the duration of the study and gained body weight.</p>	IV	A

		<u>Study deficiency:</u> The volume of water used to moisten the test substance was not provided.		
<p>Dermal sensitization/ Hartley albino guinea pig (Buehler)</p> <p>INTOX PVT. LTD. (Maharashtra, India) Study No. 18494 September 4, 2019</p> <p>OCSPP 870.2600; OECD 406</p>	51437717	<p>Is <i>not</i> a sensitizer</p> <p>20 guinea pigs (10/sex) were treated with 0.5 mL of 45% w/v (0.45 g/mL) test substance in analytical grade water containing 0.2% Tween 80 at induction and challenge; 10 control animals were treated with vehicle at induction and with 45% test substance at challenge.</p> <p>Following challenge, no positive responses (grade 1 or higher) were observed on any of the test or control animals at either time point. In a historical positive control study with α-Hexylcinnamaldehyde (40% v/v in acetone for inductions and 10% v/v in acetone for challenge), positive responses were observed on 8/20 (40%) of the positive controls at 24 and 48 hours vs. 0/10 in the vehicle controls (INTOX Study No. 18454; completed March 3, 2019).</p> <p><u>Note:</u> Suspensions with higher concentrations than 45% w/v test substance in vehicle were too thick to satisfactorily load the test patches.</p>	Negative	A

*Core Grade Key: A =Acceptable; S = Supplementary; U = Unacceptable; D = Data Gap; W = Waived